Efficacy & Safety of DNMT1 inhibitors in MEN1 Mouse model: Creating a Draft Medical Manuscript



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Introduction

- Multiple endocrine neoplasia type 1 (MEN1) is a familial cancer syndrome characterized by tumor-formation in the endocrine system
- •Previous study shows MEN1 patients having overactive DNMT1 enzyme
- •Wrote draft manuscript on project working to find potential therapy for MEN1 in a pre-clinical setting

Objective of Internship

I hoped to better understand how investigating the biology behind cancer formation could be a potential route for research, and in doing so, achieve a better understanding of how I would like to potentially approach my own independent work at the University.

Work profile

- Attend Libutti lab meetings weekly
- •Read assigned previous literature from Dr. Ziqiang Yuan's lab
- Annotate, interpret, and analyze graphs/data from the DNMT1 inhibitor project
- •Create Draft Manuscript for the DNMT1 inhibitor project

Reflection

- •During lab meetings, I learned more about approaches being used by principal investigators in their research, hear from potential collaborators, and better understand how research about health continues despite a pandemic.
- •My greatest contribution this summer was crafting a draft manuscript of the DNMT1 inhibitor project.
- The project used mouse models to understand the scope of therapies for MEN1 patients based in inhibiting the overactive DNA methyltransferase 1 (DNMT1) enzyme in a preclinical setting.

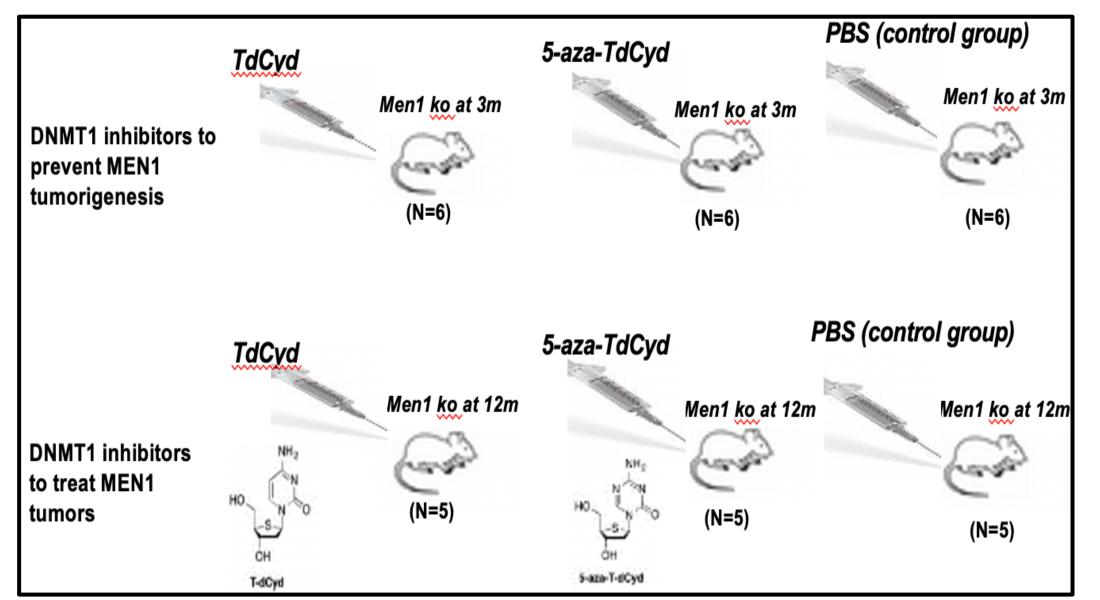


Diagram of DNMT1 inhibitor project procedure. MEN1 Knockout mice were ip-injected with one of two novel DNMT1 inhibitors (TdCyd & 5-aza-TdCyd) developed by collaborators at National Cancer Institute (NCI) and compared to a PBS control group based on two goals, figure courtesy of Dr. Ziqiang Yuan.

- •I learned about the process Dr. Yuan's lab used in approaching cancer treatment, in first finding the biological pathway of MEN1 tumors in one study and then testing a potential treatment based on this source in a pre-clinical setting.

 •I was able to see the concepts and tools
 - •I was able to see the concepts and tools described in my lectures at the University being used in a real laboratory setting to benefit global health
 - •I am immensely grateful for the guidance that I received from my advisors throughout this internship & the opportunity to be a co-author on the DNMT1 inhibitor project manuscript.

Looking ahead

- •Scientific writing and data interpretation in future
- •Developed interest in approach to cancer biology that could inspire potential route for independent work

Questions

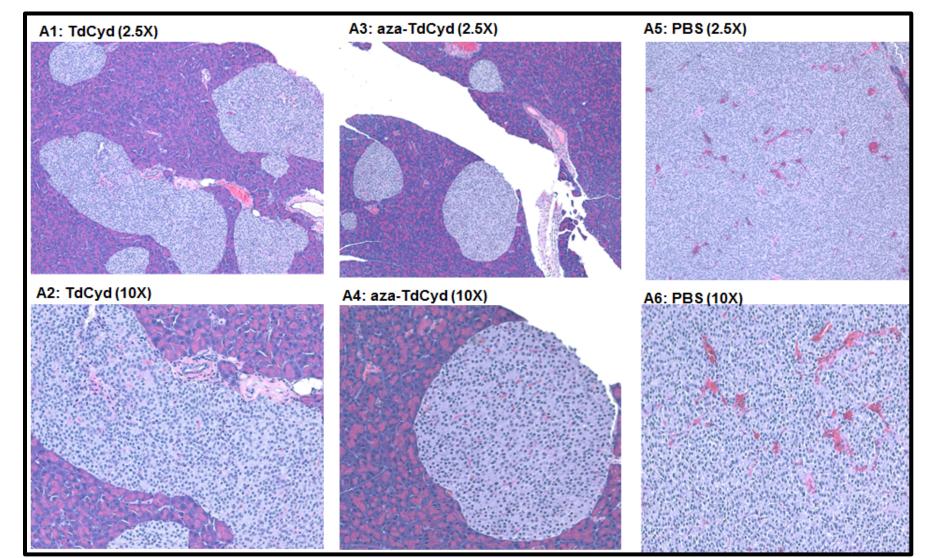
- What are the next steps in the submission process for a medical manuscript?
- •What are the next steps in using the observations made in the DNMT1 inhibitor project to move towards clinical trial?

Conclusion

Understanding potential treatment for cancers is a multistep process
Approaches that start by understanding the biology of cancer are useful to Global Health

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Example of tumor staining in MEN1 Knockout mice. Tumors treated with either DNMT1 inhibitor had smaller islets, while the PBS control group (far right) has visible insulinoma (MEN1 tumors), photo courtesy of Dr. Ziqiang Yuan.